

Cold atmospheric pressure plasma-treated liquids and formulations for cancer treatment

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Cold atmospheric pressure plasma is a partially ionized gas that has unveiled its considerable potential for cancer treatment as a new type of oncological therapy [1, 2]. The discharges are usually generated above the liquid surface, in a mixture of argon, nitrogen, and oxygen gases that facilitate the plasma generation and dictate the type of predominant reactive species that influence the effect of these irradiated liquids on normal and cancer cells [2]. It was observed that not only the gas mixture used in the discharge responsible for the selective cytotoxic effect on cancer cells, but also the chemical structure of the liquid precursor. Chitooligosaccharides, tricarballic acid, ethyl acetate, glyceric acid, and their mixture generated in plasma in certain concentrations showed a selective cytotoxic effect on cancer cells [2]. The selectivity was not induced by only one chemical compound but by a mixture of several chemicals generated in low amounts, which act synergistically.

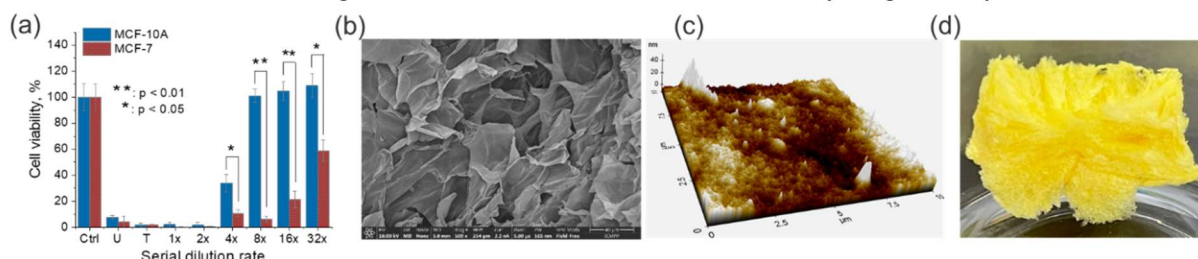


Figure 1. (a) Cell viability tests of MCF-10A (non-tumorigenic epithelial cell) and MCF-7 (breast cancer cell) lines after incubation in untreated chitosan 0.5% (U) and plasma-activated chitosan (T) solution. (b) and (c) SEM and AFM of plasma-activated chitosan-based hydrogel, respectively. (d) Photo of xerogel obtained from plasma-activated chitosan reticulated with natural mono-aldehyde.

Therefore, the plasma-activated liquids provide a foundation for clinical applications of combinatorial chemistry to enhance selectivity during therapy, offering patients a more effective and less harmful option. This also paves the way for engineering liquids by plasma for drug delivery systems, such as plasma-activated-based hydrogels, to preserve and improve bioavailability, and serve as a platform to deliver the plasma-activated liquid content to cells.

[1] H. Tanaka, M. Mizuno, K. Ishikawa, C. Miron, Y. Okazaki, S. Toyokuni, K. Nakamura, H. Kajiyama, M. Hori, *Free Radical Research* **57** (2023) 14-20.

[2] C. Miron, B. Andreica, M. Iftime, A. Fifere, T. Yamakawa, S. Toyokuni, M. Mizuno, L. Mititelu-Tartau, Y. Motooka, A. Bejan, T. Kondo, I. Sava, V. Harabagiu, J. Kumagai, A. Tanaka, H. Tanaka, L. Marin, M. Hori, *International Journal of Biological Macromolecules*, **281**, 136513 (2024) 1-16.